Serial No. 09/537,654
Group Art Unit: 1638

REMARKS

Reconsideration of the present application is respectfully requested. Claims 2-10, 12, and 14-35 are pending. Claim 13 has been cancelled without prejudice. Support for these claims is found in the claims as originally filed, and throughout the specification. No new matter has been added.

The Examiner has objected to the amended title "Rad51-Like Orthologues and Uses Thereof" stating that it is not descriptive of the instant invention drawn to a RAD51 gene, not to the protein. Applicants presume the term objected to in the title is "orthologue" and respectfully disagree that this is not a proper descriptive term. However, in order to expedite prosecution, Applicants have amended the title to replace the term "orthologues" with the term "polynucleotides". Applicants believe this amendment obviates the objection and respectfully request this objection be withdrawn, or if the objection has been misinterpreted, that the Examiner clarify by specifically identifying the objectionable term or phrase.

Claims 2, 4, 8, 9, 12, 14 and 15 have been amended.

Claims 2, 4, 9, 12, and 15 have been amended to correct informalities regarding improper definite articles.

Claim 8 has been amended to make explicit what was implicit in the original claim. Specifically, as amended claim 8 recites "wherein the seed comprises the recombinant expression cassette".

Claim 12 has been amended to recite "wherein the sequence encodes a polypeptide which participates in a complex which enhances recombinase activity". Amended Claim 14 and new claim 25 also recite this function. Support for this amendment can be found on page 1, line 33 – page 4, line 11, particularly page 2, line 32 – page 3, line 2 of the specification and in the claims as originally filed.

Claim 14 has been amended to make explicit what was implicit in the original claim. Specifically, as amended claim 14 recites specific high stringency hybridization conditions. Claim 14 has also been amended to recite a polynucleotide

which selectively hybridizes to the full-length complement of SEQ ID NO: 1. Support for these amendments can be found on page 16, lines 11-13 and page 29, lines 15-17 of the specification.

New claims 16-35 have been added. No new matter has been introduced by the addition of these claims which find support in the specification and claims as originally filed.

New claims 16 and 17 are dependent on claim 12 and recite further limits to the claimed percent sequence identity. Support for these claims can be found in original claim 1, and page 29, lines 1-4 of the specification.

New claims 18-24, and 28-34 are similar to original and amended claims 2-8 and depend from claim 14 and claim 25 respectively. These claims find support in claims 2-8 and in the specification as originally filed.

New claim 25 claims a polynucleotide which encodes a polypeptide having at least 90% sequence identity over the entire length of SEQ ID NO: 2, wherein the polypeptide participates in a complex which enhances recombinase activity. Support for this claim can be found on page 7, line 12 – page 9, line 3; page 20, line 7 – page 21, line 8; page 25, line 26 – page 26, line 6; and page 45, lines 28-33, as well as the support cited above for claims 12 and 14.

New claims 26 and 27 are dependent on new claim 25 and recite further limits to the claimed percent sequence identity. Support for these claims can be found on page 45, lines 28-33 of the specification.

New claim 35 claims a polynucleotide comprising a nucleic acid sequence which encodes at least 25 contiguous amino acids of SEQ ID NO: 2. Support for this claim can be found on page 30, lines 10-12 of the specification.

The marked up version of these amendments is found on a separate sheet attached to this amendment and titled "**Version with Markings to Show Changes Made.**" It is respectfully requested that the amendments be entered.

Serial No. 09/537,654
Group Art Unit: 1638

Rejections under 35 U.S.C. §101:

Claim 14 is rejected under 35 U.S.C. §101 as not having either a credible asserted utility or a well-established utility.

The Examiner asserts that isolated polynucleotides of at least 100 contiguous nucleotides that selectively hybridize to SEQ ID NO: 1 include a human DNA repair protein (1998, GenBank AI184177), and that the instant specification does not teach a specific use of these nucleic acids.

Claim 14 has been amended to recite a sequence which selectively hybridizes to the full-length complement of SEQ ID NO: 1 under explicitly recited specific high stringency conditions, "wherein the sequence encodes a polypeptide which participates in a complex which enhances recombinase activity". Support for this amendment can be found on page 1, line 33 – page 4, line 11, particularly page 2, line 32 – page 3, line 2 of the specification. Further support is found in references A6 and A7 contained in the IDS submitted 6/23/00. In these references, Sung demonstrates the activity of the purified eukaryotic recombinase Rad51 (ref. A6), and the enhancement of recombinase activity in the presence of the members of the Rad52 epistasis group, the Rad55/Rad57 complex (ref. A7). Thacker (ref. A20 submitted 12/21/00) shows in Figure 2, page 167, that the Rad51-like homologue Rad51L2 (Rad51C) is most similar to yeast Rad57.

Page 15, lines 1-3 of the specification notes that "Selectively hybridizing sequences typically have about at least 80% sequence identity, preferably 90% sequence identity, and most preferably 100% sequence identity (i.e., complementary) with each other." The sequence disclosed in GenBank AI184177 does not have a long region of sufficient complementarity with SEQ ID NO: 1, such that it would be capable of selectively hybridizing to the full-length complement of SEQ ID NO:1 under the conditions listed in the amended claim. As amended, claim 14 does require utility as disclosed in the specification. This amendment obviates the rejection.

The Examiner maintains the rejection of claim 8 under 35 U.S.C. §101 as not having a specific or well-established utility because the claim does not require that the transgenic seed have the expression cassette of claim 2.

Claim 8 has been amended, as recommended by the Examiner, to recite "wherein the seed comprises the recombinant expression cassette". This amendment obviates the rejection.

Applicants have properly addressed the grounds for the rejection of claims 14 and 8 under 35 U.S.C. §101 and respectfully request that the rejection of the claims under 35 U.S.C §101 be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph – Utility:

Claim 14 is rejected under 35 U.S.C. §112, first paragraph as the claimed invention lacks utility, therefore one of skill in the art would not know how to use the invention.

As the Applicants have responded to the utility rejection under 35 U.S.C. §101, it is believed that the utility rejection has been overcome. As amended the claim requires utility, the polynucleotide "encodes a polypeptide which participates in a complex which enhances recombinase activity". As this rejection could have been asserted against claim 8, Applicants believe that the amendment to claim 8 has obviated the rejection under 35 U.S.C. §101, and therefore a rejection under 35 U.S.C. §112, first paragraph should not be applied to amended claim 8.

Therefore, it is respectfully requested that the concomitant rejection of claim 14 under 35 U.S.C. §112, first paragraph based on a lack of utility be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph:

The Examiner states "Claims 2-10 and 12-15 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO: 1 or that encode SEQ ID NO: 2, does not reasonably provide enablement for nucleic acids that have 80% identity to SEQ ID NO: 1, that are

amplified from primers that hybridize under unspecified stringency to 'loci within' SEQ ID NO: 1, or that comprise 100 nucleotides that hybridize to SEQ ID NO: 1."

Applicants have amended claim 12 to recite sequences having at least 90% sequence identity over the entire length of SEQ ID NO: 1. Applicants have cancelled claim 13, directed to amplified polynucleotides. Applicants have amended claim 14, which now claims sequences which selectively hybridize to the full-length complement of SEQ ID NO: 1 under explicit high stringency conditions. Both amended claims 12 and 14 further recite the function for the polynucleotides claims in that they encode a polypeptide which participates in a complex which enhances recombinase activity.

As is stated in MPEP 2164.01 "A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)."

Further, Applicants submit that the specification is not required to disclose all possible permutations as defined by the limitations of the claims. The specification is required to provide sufficient disclosure and enablement so that one skilled in the art could make the embodiments encompassed by the claims. "It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art . . ." *In re Vaek*, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991).

As pointed out in the response filed 15 April, 2002, the present application and the knowledge in the art provides sufficient information and guidance to enable one of skill in the art to make and use a polynucleotide with at least 90% sequence identity to SEQ ID NO: 1, or that selectively hybridizes to SEQ ID NO: 1 under the stringent conditions presented in amended claim 14. The disclosure does not teach the "mere germ of an idea", the disclosure teaches three independent full length

Rad51C polynucleotide sequences and teaches one of skill in the art methods to isolate, make, modify and identify polynucleotides with 90% sequence identity to SEQ ID NO: 1, or that selectively hybridize to SEQ ID NO: 1 under the proscribed conditions. While the Examiner dismisses the extensive guidance in the specification pointed to in the response filed 15 April 2002 as "general", this guidance is sufficient to enable one of skill in the art to readily make the embodiments encompassed by the claims.

The Examiner asserts that undue experimentation would have been required by one skilled in the art to practice the invention. The Examiner contends one would have to make all the possible single amino acids substitutions and analyze the greater than 19^{294} nucleic acids generated. The Examiner also asserts undue trial and error would be required to screen through all the plants transformed with the polynucleotides encompassed by the present invention.

The Applicants respectfully disagree. It is not necessary to make and assay every possible substitution in order to obtain a polynucleotide that encodes a polypeptide which participates in a complex which enhances recombinase activity, one or a few variants will suffice. The question of experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is the amount of experimentation must not be unduly extensive. *PPG Inc. v. Guardian Industries Corp.* (37 USPQ 1218, 1623, (Fed. Cir. 1996). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (1982 PTOBA).

Claims 12, 14 and 15 have been amended to claim polynucleotides "which encode a polypeptide which participates in a complex which enhances recombinase activity". As noted above, Applicants have disclosed several sequences (SEQ ID

NOS: 1-6), provided guidance regarding modifications to the sequences, methods to analyze, isolate, identify and characterize the sequences. The 3-dimensional structure of related proteins were known in the art at the time of filing, as well as methods to assay for functional RAD51 homologues and mediators of recombinase activity (refs. A6 and A7 submitted 6/23/00). Although techniques for expressing, monitoring, and purifying polypeptides are well-known in the art, additional disclosure can be found on pages 29–31, pages 46-49, and page 52 of the specification. Therefore screening for the polynucleotides and polypeptides of the present invention, either structurally or functionally, is routine experimentation.

Applicants have provided reasonable guidance such that one of skill in the art can practice the breadth of the invention as disclosed and claimed, therefore the rejection of claims 2-10, 12, 14, and 15 under 35 U.S.C. §112, first paragraph should be withdrawn and not applied to new claims 16-35.

Claims 2-10 and 12 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant are that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to specific polynucleotides having a predictable structure represented by their sequence identity to SEQ ID NO: 1. In this way, Applicants have conceived the sequences of the invention as articulated in *Amgen v. Chugai Pharm.*; that is, Applicants are able "to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it." *Amgen, Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991), *cert. denied*, 112 S. Ct. 169 (1991).

The polynucleotide claims further recite a functional characteristic, that they encode a polypeptide which participates in a complex which enhances recombinase activity. The written description requirement may also be satisfied by a recitation of functional characteristics. For example, on page 53 of the *Revised Interim Written Description Guidelines*, Example 14 is directed to a generic claim of a protein having

high sequence identity to the sequence of SEQ ID NO: 3, "wherein the sequence catalyzes the reaction A -> B." The Guidelines concludes that the generic claim of Example 14 is sufficiently described under §112, first paragraph because:

1) the single sequence disclosed in SEQ ID NO: 3 is representative of the genus, and

2) the claim recites a limitation requiring the compound to catalyze the reaction from A-> B.

Thus, on the basis of the limitations provided in Example 14, one of skill in the art would recognize that the patentee was in possession of the necessary common attributes possessed by the members of the genus. In the instant case, the amended claims all require the functional limitation that the claimed polynucleotides comprise sequences which encode a polypeptide which participates in a complex which enhances recombinase activity.

Applicants have sufficiently described by way of structural, chemical, and functional characteristics the polynucleotides of the present invention to reasonably convey to one of skill in the art that the Applicants were in possession of the invention at the time of filing.

The Examiner states: "Neither the instant specification nor the originally filed claims appear to provide support for the phrase 'over the entire length of the reference sequence' in claim 12." Applicants point to page 17, line 32 – page 18, line 2 and page 20, lines 8-10 of the specification, which support the use of this phrase. Therefore, this phrase does not constitute new matter. However, Applicants have amended claim 12 to read "90% sequence identity over the entire length of SEQ ID NO: 1" in order to clarify the claim. Applicants believe this amendment obviates this rejection of claim 12.

In light of the amendments and arguments presented above, Applicants respectfully request that the rejection of claims 2-10, 12, 14 and 15 under 35 U.S.C §112 first paragraph be withdrawn, and that the rejection not be applied to new claims 16-35.

Serial No. 09/537,654
Group Art Unit: 1638

Rejections under 35 U.S.C. §112, second paragraph:

Claims 2-10 and 12-14 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

Claim 13 has been cancelled without prejudice. Claim 14 has been amended to explicitly recite specific high stringency hybridization conditions. As stated in the response filed April 15, 2002, the term "selectively hybridizes" is defined in the specification. Coupled with the recitation of specific stringent hybridization conditions, Applicants believe the claim is definite. The role of wash conditions is discussed on pages 16-17. While temperature and ionic strength are viewed as important factors, the time of the wash, in general is not. Claim 14 defines the *important* wash parameters of ionic strength and temperature as 0.1X SSC at 60°C. Ausubel, *et al.* review the important parameters for hybridization in chapter 2.10 of Volume 1 *Current Protocols in Molecular Biology* (1995, Greene Publishing and John Wiley and Sons). In particular, see pages 2.10.8 – 2.10.15 which review the parameters important to sensitivity and specificity and provides a troubleshooting guide. As is stated on page 2.10.10, column 2, paragraph 2 "Specificity is the function of post-hybridization washes, the critical parameters being the ionic strength of the final wash solution and the temperature at which this wash is carried out." Further discussion regarding troubleshooting lack of specificity point to changing the ionic strength, or the temperature at which the wash is done, not the time of the wash. Therefore, Applicants believe recitation of a particular time for which the wash is done is unnecessary.

Applicant has addressed the rejections under 35 U.S.C. §112, second paragraph by proper amendments and arguments. Claims 2-10, 12, 14 and 15, and new claims 16-35 are in proper form, therefore Applicant respectfully requests the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

Serial No. 09/537,654
Group Art Unit: 1638

Rejections under 35 U.S.C. § 102:

Claim 14 is rejected under 35 U.S.C. §102(a) as being anticipated by NCI-CGAP (1998, GenBank Accession No. AI184177) for reasons of record. The Examiner asserts the nucleic acid taught by NCI-CGAP would selectively hybridize to SEQ ID NO: 1.

Claim 14 has been amended and now claims a sequence which selectively hybridizes under explicitly recited high stringency hybridization conditions to the full-length complement of SEQ ID NO: 1. Page 15, lines 1-3 of the specification notes that "Selectively hybridizing sequences typically have about at least 80% sequence identity, preferably 90% sequence identity, and most preferably 100% sequence identity (i.e., complementary) with each other." The sequence disclosed in GenBank AI184177 does not have a long region having at least 80% sequence identity with SEQ ID NO: 1 such that it would be capable of selectively hybridizing to the full-length complement of SEQ ID NO:1 under the conditions recited, thereby obviating the rejection.

Applicants respectfully request that the rejection of claim 14 under 35 U.S.C. § 102(a) be withdrawn.

Serial No. 09/537,654
Group Art Unit: 1638

CONCLUSION

In light of the foregoing remarks and amendments, withdrawal of the outstanding rejections and allowance of all of the remaining claims is respectfully requested. Applicants believe that the claims are in condition for allowance. The Examiner is invited to telephone the Applicant in order to expedite prosecution of the application.

Respectfully submitted,

Virginia Dress

Virginia Dress
Agent for Applicant(s)
Registration No. 48,243

PIONEER HI-BRED INTERNATIONAL, INC.
Corporate Intellectual Property
7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000
Phone: (515) 270-4192
Facsimile: (515) 334-6883

Serial No. 09/537,654
Group Art Unit: 1638

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The Applicants have used underlining to denote additions to the original text and square brackets [ ] to denote deletions of the original text.

In the Title:

The title found on the cover page has been amended as follows:

Rad51-Like [Orthologues] Polynucleotides and Uses Thereof

In the Claims:

Claim 13 has been cancelled.

Claims 2, 4, 8, 9, 12, 14 and 15 have been amended as follows:

2. (Twice Amended) A recombinant expression cassette comprising [a member] the polynucleotide of claim 12 operably linked to a promoter.

4. (Amended) A transgenic plant comprising [a] the recombinant expression cassette of claim 2.

8. (Amended) A transgenic seed from the transgenic plant of claim 4, wherein the seed comprises the recombinant expression cassette.

9. (Twice Amended) A method of modulating the level of RAD51C in a plant, comprising:

(a) introducing into a plant cell a recombinant expression cassette comprising [a] the polynucleotide of claim 12 operably linked to a promoter;

(b) culturing the plant cell under plant cell growing conditions;

(c) regenerating a whole plant which possesses the transformed genotype; and

(d) inducing expression of said polynucleotide for a time sufficient to modulate the level of RAD51C in said plant.

12. (Amended) An isolated polynucleotide [encoding a polypeptide with Rad51C activity comprising a member] selected from the group consisting of:

(a) a [polynucleotide] nucleic acid sequence having at least [80%] 90% sequence identity over the entire length of [the reference sequence] SEQ ID NO: 1, as determined by the GAP program under default parameters, [to a polynucleotide of SEQ ID NO: 1] wherein said sequence encodes a polypeptide which participates in a complex which enhances recombinase activity; and

(b) [a polynucleotide encoding a polypeptide of SEQ ID NO: 2;

(c) a polynucleotide of SEQ ID NO: 1;]

[(d)] a [polynucleotide] nucleic acid sequence which is fully complementary to [a] the [polynucleotide] nucleic acid sequence of (a)[, (b), or (c)].

14. (Amended) An isolated polynucleotide comprising a nucleic acid sequence [at least 100 contiguous nucleotides] which selectively hybridizes to the full-length complement of SEQ ID NO: 1, under stringent hybridization conditions and a wash in 0.1X SSC at 60°C, [to a polynucleotide of SEQ ID NO: 1,] wherein stringent hybridization conditions comprise 50% formamide, 1M NaCl, and 1% SDS at 37°C, and wherein the sequence encodes a

polypeptide which participates in a complex which enhances recombinase activity.

15. (Amended) An isolated polynucleotide comprising at least 50 contiguous nucleotides from [a] the polynucleotide of SEQ ID NO: 1.

New claims 16-35 have been added as follows:

16. The isolated polynucleotide of claim 12, wherein the nucleic acid sequence of (a) has at least 95% sequence identity to SEQ ID NO: 1.

17. The isolated polynucleotide of claim 12, wherein the polynucleotide is SEQ ID NO: 1.

18. A recombinant expression cassette comprising the polynucleotide of claim 14 operably linked to a promoter.

19. A host cell comprising the recombinant expression cassette of claim 18.

20. A transgenic plant comprising the recombinant expression cassette of claim 18.

21. The transgenic plant of claim 20, wherein said plant is a monocot.

22. The transgenic plant of claim 20, wherein said plant is a dicot.

23. The transgenic plant of claim 20, wherein said plant is selected from the group consisting of maize, soybean, sunflower, sorghum, canola, wheat, alfalfa, cotton, rice, barley, and millet.

24. A transgenic seed from the plant of claim 20, wherein the seed comprises the recombinant expression cassette.

25. An isolated polynucleotide comprising a member selected from the group consisting of:
(a) a nucleic acid sequence encoding a polypeptide having at least 90% sequence identity over the entire length of SEQ ID NO: 2, as determined by the GAP algorithm under default parameters, wherein the encoded polypeptide participates in a complex which enhances recombinase activity; and
(b) a nucleic acid sequence which is fully complementary to the nucleic acid sequence of (a).

26. The isolated polynucleotide of claim 25, wherein the nucleic acid sequence of (a) encodes a polypeptide having at least 95% sequence identity to SEQ ID NO: 2.

27. The isolated polynucleotide of claim 25, wherein the nucleic acid sequence of (a) encodes the polypeptide of SEQ ID NO: 2.

28. A recombinant expression cassette comprising the polynucleotide of claim 25 operably linked to a promoter.

29. A host cell comprising the recombinant expression cassette of claim 28.

30. A transgenic plant comprising the recombinant expression cassette of claim 28.

31. The transgenic plant of claim 30, wherein said plant is a monocot.

32. The transgenic plant of claim 30, wherein said plant is a dicot.

33. The transgenic plant of claim 30, wherein said plant is selected from the group consisting of maize, soybean, sunflower, sorghum, canola, wheat, alfalfa, cotton, rice, barley, and millet.

34. A transgenic seed from the plant of claim 30, wherein the seed comprises the recombinant expression cassette.

35. An isolated polynucleotide comprising a nucleic acid sequence which encodes at least 25 contiguous amino acids of SEQ ID NO: 2.